# OVERCOMING BARRIERS TO EVIDENCE GENERATION FOR GENOMIC DIAGNOSTIC TESTS

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# EGAPP Working Group
## (Teutsch et al, Genet Med, 2008)

- "Of most concern, the number and quality of studies are limited. Test applications are being proposed and marketed based on descriptive evidence and pathophysiologic reasoning, often lacking well-designed clinical trials or observational studies to establish validity and utility, but advocated by industry and patient interest groups"

# The Evidence Paradox

- 18,000+ RCTs published each year
- Tens of thousands of other clinical studies
- Systematic reviews intended to inform clinical and health policy decisions routinely conclude that evidence is insufficient

# Studying the Right Questions

- Gaps in evidence reflect insufficient engagement of decision makers (patients, clinicians, payers) in selecting research questions

# Compromise on Methods

- Many CER studies will require a conscious decision to sacrifice internal validity in order to increase generalizability, relevance, feasibility and timeliness
- The right balance is not a scientific issue, it's a social judgment about an acceptable level of uncertainty, involving multiple stakeholders
- Process to achieve this not yet well defined

# Managed Entry Agreements

HTAi Policy Forum Definition*

> "an arrangement between a manufacturer and payer/provider that enables access to....a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact"

*Klemp, M et al (in press) What principles should govern the use of managed entry agreements? International Journal of Technology Assessment in Health Care

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# SACGHS recommendation

- "Information on clinical utility is critical for managing patients, developing professional guidelines, and making coverage decisions."
- "HHS should create a public private entity of stakeholders to….establish evidentiary standards and levels of certainty required for different situations"

# PCORI Methodology Committee

- "…shall work to improve the science and methods of comparative clinical effectiveness research by…"
- Developing and updating methodological standards that "shall provide specific criteria for internal validity, generalizability, feasibility and timeliness of research…"

# PCORI Methods - Process

- "The process for developing and updating such guidance shall include input from all relevant experts, stakeholders, and decision makers, and shall provide opportunities for public comment."

# Methodological Guidance for CER

- "Effectiveness Guidance Documents"
- Analogous to FDA-guidance
- Recommendations for study design reflecting information needs of patients, clinicians, payers
- Targeted to product developers, clinical researchers
- Objective is to provide "reasonable confidence of improved health outcomes"
- Balance validity with relevance, feasibility, timeliness

# Review Methods vs Guidance

- Teutsch (Table 4): "What was the relative importance of outcomes measured; which were pre-specified primary outcomes and which were secondary"
- CMTP EGD: "Valid outcomes or surrogates for breast cancer prognosis include distant recurrence at 5 or 10 years, disease free survival, disease specific mortality, and overall survival"

# EGD Development Process

- Begin with systematic reviews, HTA, etc
- Content experts generate initial draft recommendations
- Technical working group refines draft recs
- Expert - stakeholder advisory group meeting to discuss draft recommendations
- Revised recs circulated for public comment
- Final methods recommendations posted